

右美沙芬用于 80 例胆囊切除术后镇痛的临床观察与分析

郭正纲 苏小军[△] 靳 恒 贾晓鹏

(解放军总医院第一附属医院麻醉科 北京 100048)

摘要 目的 观察和分析右美沙芬用于 80 例胆囊切除术的超前镇痛作用临床疗效。方法 将 2009 年 8 月~2011 年 11 月我院接收并确诊的 80 例 ASA ~ 级择期行腹腔镜胆囊切除手术患者,按患者意愿随机分为两组。治疗组 40 例,麻醉诱导前 30min 肌注右美沙芬 20mg;对照组 40 例,麻醉诱导前 30min 肌注等量生理盐水。术中监测患者的血氧饱和度值、心率、平均动脉压等;术后统计术中(除麻醉诱导外)镇痛药的用量,并对患者伤口疼痛进行 VAS 评分。结果 对照组术中镇痛药(除麻醉诱导外)用量大于治疗组,但二者无统计学差异($P>0.05$),术后伤口无痛者治疗组明显多于对照组,治疗组 VAS 评分显著低于对照组,差异有统计学意义($P<0.01$)。结论 右美沙芬对于胆囊切除术有超前镇痛的作用,麻醉诱导前 30 min 肌注 20mg,不仅可以减少术中镇痛药的用量,而且在更大程度上减轻了术后患者伤口的疼痛。

关键词 右美沙芬;胆囊切除术;超前镇痛;临床

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Observation and Analysis on Analgesia after Cystic Resection of 80 Cases with the Dextromethorphan

GUO Zheng-gang, SU Xiao-jun[△], JIN Heng, JIA Xiao-peng

(Department of Anesthesiology, the First Hospital Affiliated to the Chinese PLA Hospital, Beijing, 100048)

ABSTRACT Objective: To observe and analyze clinical curative effect of analgesia after cystic resection of 80 cases with the dextromethorphan. **Methods:** Divide 80 cases of ASA ~ from August 2009 to November 2011 received and diagnosed in laparoscopic gallbladder surgery patients into two groups, randomly according to the patients' will. The treatment group in 40 cases, intramuscular inject dextromethorphan 20 mg before narcotic induction 30 min; The control group in 40 cases, intramuscular inject amount saline before narcotic induction 30 min. To monitor patients' aorta pressure, heart rate, oxygen saturation values, etc during the operation. Statistics intraoperative (except the narcotic induction) analgesic drug dosage after the operation, and the wound on patients with pain VAS score. **Results:** The control group intraoperative analgesics (except the narcotic induction) dosage is greater than the treatment group, but not statistical difference ($P>0.05$). The treatment group postoperative wound the painless significantly more than the control group, and the treatment group VAS score significantly lower than those of the control group, and the difference was statistically significant ($P<0.01$). **Conclusion:** The dextromethorphan for cystic resection has the role of preemptive analgesia. Intramuscular injecting 20 mg before 30 min narcotic induction can not only reduce the dosage of intraoperative analgesics, but also reduce the postoperative patients wound of pain in greater extent.

Key words: Dextromethorphan; Cholecystectomy; Preemptive Analgesia; Clinical Effects

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腹腔镜胆囊切除术后,患者内脏神经反射的表现为肩背部的放射性疼痛,往往比腹壁钻孔疼痛更为明显^[1]。超前镇痛是近年来在麻醉领域中提出的一种新概念,是一种在伤害性刺激作用于机体之前采取的可以防止神经中枢敏化,减少和消除伤害引起疼痛的治疗措施^[2-3]。在近几年国内外文献报道中,对于右美沙芬增强术中、术后的镇痛实验研究已有较明确的成果,但是用于临床上的案例并不广泛^[4]。右美沙芬是可待因的右旋异构体,临床主要作为镇咳药使用,具有特殊的中枢镇咳作用^[5]。

研究发现右美沙芬是低亲和力、非特异性 NMDA 受体拮抗剂,可抑制兴奋性氨基酸与 NMDA 受体的结合,阻止中枢神经敏化形成,并减轻后续疼痛程度而起到超前镇痛的作用。本临床研究旨在探讨右美沙芬在胆囊切除术后镇痛中的应用^[6-7]。

1 临床资料

1.1 一般资料

选取我院 2009 年 8 月~2011 年 11 月接收确诊的 80 例 ASA ~ 级择期行腹腔镜胆囊切除手术患者,按患者意愿随机分为 2 组。治疗组 40 例,年龄 22~71 岁,男 18 例,女 22 例,体重指数 20~22;对照组 40 例,年龄 23~69 岁,男 19 例,女 21 例,体重指数 21~22。两组患者在年龄、性别和体重指数上的差异无统计学意义($P>0.05$),具有可比性。

1.2 病例排除标准

作者简介 郭正纲(1979-)男,硕士,主治医师,研究方向为麻醉药理

△通讯作者 苏小军(1969-)男,博士,副主任医师,研究方向为麻醉药理

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①右美沙芬禁忌症者；②6个月内有消化道溃疡病史者；③肝肾功能障碍者；④有出血性疾病者，血小板计数减少者；⑤术前1周内使用过非甾体类抗炎药、阿片类镇痛药和单胺氧化酶抑制剂的患者；⑥孕妇。

2 方法

2.1 麻醉方法

①术前麻醉处理：所有患者术前30 min均肌注苯巴比妥钠0.1 g、阿托品0.5 mg，均按全麻常规进行术前准备。②麻醉诱导前30 min，治疗组肌注右美沙芬20 mg，对照组肌注等量生理盐水。③麻醉诱导：所有患者均依次静注咪达唑仑0.05 mg/kg、维库溴铵0.1 mg/kg、丙泊酚1.5 mg/kg、瑞芬太尼2 μ g/kg，待药物充分起效(约2 min)后气管插管机械通气。④维持麻醉：术中以丙泊酚4~6 mg/(kg·h)、瑞芬太尼0.1~0.3 μ g/(kg·min)、维库溴铵间断静注。⑤术毕常规用药。苏醒期躁动者静注芬太尼0.5 μ g/kg。

2.2 观测指标

①采用 Philips 多功能监护仪，常规连续监测平均动脉压(MAP)、血氧饱和度(SpO₂)、心率(HR)、心电图等。②统计术中(除麻醉诱导外)镇痛药(丙泊酚和瑞芬太尼)的用量。③采用VAS评分来评价疼痛：VAS评分为0~10，疼痛程度依次增大，0分为无痛，10分为剧痛。由此来评价镇痛效果，<3分为优，3~5分为良，≥5分为差。记录术后0、1、2、4、8、12、24 h两组患者的VAS评分。

2.3 统计学处理

所有数据采用 SPSS 13.0 统计学软件进行处理。计量资料以均数±标准差($\bar{x} \pm s$)表示，采用两组间比较的 t 检验进行统计学处理，计数资料比较用 X² 检验，P<0.05 为差异有统计学意义，P<0.01 为差异极具统计学意义。

3 结果

3.1 两组患者一般情况比较

表 1 两组患者一般情况比较
Table 1 Generally comparison of the two groups

Group	Number of people	Age	Body Mass Index	Time
Treatment group	40	42.3± 12.0	21.2± 1.0	72.3± 25.9
Control group	40	43.1± 11.7	20.6± 0.9	73.1± 24.8

由表 1 可得，两组患者的年龄、体重及手术持续时间比较均无显著性差异(P>0.05)。

3.1 两组患者术中镇痛药用量的比较

术后统计术中(除麻醉诱导外)的镇痛药用量，见表 2。

表 2 术中镇痛药用量($\bar{x} \pm s$)
Table 2 Intraoperative analgesics dosage($\bar{x} \pm s$)

Group	Number of people	Propofol [mg/(kg·h)]	Remifentanyl [g/(kg·h)]
Treatment group	40	2.9± 0.5	5.4± 1.9
Control group	40	3.5± 1.2	6.8± 2.4

由表 2 可得，治疗组患者术中(除麻醉诱导外)镇痛药的用量小于对照组，但二者间无显著性差异(P>0.05)，说明右美沙芬用于胆囊切除术在术中镇痛药用量方面并无显著性的优势。

3.2 两组患者术后 VAS 评分比较

记录术后 0、1、2、4、8、12、24 h 两组患者的 VAS 评分，见表 3。

表 3 术后各时点 VAS 评分($\bar{x} \pm s$)
Table 3 VAS score of each point after operation($\bar{x} \pm s$)

Group	Number of people	0h	1h	2h	4h	8h	12h	24h
Treatment group	40	0.3± 0.1	0.4± 0.2	0.7± 0.2	0.6± 0.1	0.3± 0.4	0.3± 0.3	0.2± 0.4
Control group	40	2.3± 1.2	2.4± 1.1	2.6± 0.9	2.3± 0.6	2.1± 1.2	1.6± 0.7	0.9± 1.4

由表 3 可得，治疗组在术后各时点的 VAS 评分均显著低于对照组，差异极具统计学意义(P<0.01)。说明治疗组患者在手术后的疼痛感明显轻于对照组患者，对临床治疗效果有很大帮助。

4 讨论

目前临床上主要应用传统的阿片类药物和非甾体类抗炎药来控制围手术期疼痛，但阿片类药物普遍存在呼吸抑制作

用,也有可能导致恶心、过度镇静、便秘、呕吐等不良反应,而非甾体类抗炎药大多有不同程度的出血倾向,并有可能产生肾功能损害,二者均因副作用多而限制了使用。右美沙芬是可待因的右旋异构体,临床主要作为镇咳药使用,具有特殊的中枢镇咳作用。其本身并无镇痛功能,无法减轻急性疼痛^[8-11],临床上不单独使用作为镇痛药。但研究发现右美沙芬是低亲和力、非特异性 NMDA 受体拮抗剂,可抑制兴奋性氨基酸与 NMDA 受体的结合,阻止中枢神经敏感化形成,并减轻后续疼痛程度而起到超前镇痛的作用^[12]。右美沙芬作为 NMDA 受体拮抗剂,能够广泛与中枢神经系统的 NMDA 受体结合,竞争性抑制 NMDA 受体活性,减少 NMDA 受体 Ca^{2+} 内流,还可以调节电压依赖性 Ca^{2+} 通道的激活。许多国外的基础研究及临床应用均提示右美沙芬可提高痛阈,改善疼痛状态,提高生活质量。有文献报道,右美沙芬临床运用优势之一就是可配合阿片类镇痛药一起使用发挥超前镇痛的作用,在伤害刺激前给药,即可降低对机体疼痛的敏感性,也可减少术后其他镇痛药的需求量及副作用^[13]。另有报道术前应用右美沙芬可以阻止脊髓伤害性神经元的敏感化,产生超前镇痛作用^[14-16]。在国内外临床应用研究综述中有学者认为右美沙芬属于安全的非麻醉性药物^[7]。有研究结果显示,为明显减少阿片类药物的用量,且减少不良反应,可于手术前或手术后肌注右美沙芬^[17]。张学康等^[18]通过临床实验证实右美沙芬用于超前镇痛,以 20 mg 为最佳剂量。右美沙芬可改善疼痛状态,其起效时间约为 30 min,因此在麻醉诱导前 30 min 用药可减少术中全麻药和止痛药的用量^[19-20]。故本实验采用术前 30min 肌注 20mg 右美沙芬作为治疗组的治疗方法。

在腹腔镜胆囊切除手术中,临床上普遍使用瑞芬太尼作为术中镇痛麻醉药,但其消除半衰期只有 9.5 min,在停药后血浆药物浓度很快下降,患者在苏醒时会很快感到伤口的疼痛^[21-22]。本实验采用 20mg 肌注右美沙芬作为研究治疗的方法,与肌注等量生理盐水作为对比,术中的镇痛药用量治疗组少于对照组,但无显著差异($P>0.05$);术后各时点 VAS 评分治疗组显著小于对照组,差异极具统计学意义($P<0.01$)。

综上所述,右美沙芬对于胆囊切除术有超前镇痛的作用,麻醉诱导前 30 min 肌注 20mg,不仅可以减少术中镇痛药的用量,而且在更大程度上减轻了术后患者伤口的疼痛。由于右美沙芬与 NMDA 受体亲和力较低,从而不良反应少。右美沙芬的使用减少了手术期镇痛药的用量,从而减少了用其带来的不良反应,这是右美沙芬超前镇痛的临床运用优势之一。

参考文献(References)

- [1] Allergy and Immunology[J]. China Medical Abstracts(Internal Medicine), 2010, (01):98-100
- [2] Han Ze-Guang Shanghai-MOST Key Laboratory for Disease and Health Genomics, Chinese National Human Genome Center at Shanghai, Shanghai 201203, China. Recent progress in 8igenomic research of liver cancer[J]. Science in China(Series C:Life Sciences), 2009(01):46-47
- [3] Jin Feng-liang, Dong Xiao-lin, Xu Xiao-xia. cDNA cloning and recombinant expression of the general odorant binding protein from *Spodoptera litura*[J]. Science in China(Series C:Life Sciences), 2009, (01):277-279
- [4] Shen H, He MM, Liu H, et al. Comparative metabolic capabilities and inhibitory profiles of CYP2D6.1, CYP2D6.10 and CYP2D6.17[J]. Drug Metab Dispos, 2008, (05):40-42
- [5] Li D, Kerns EH, Li SQ, et al. Comparison of cytochrome P450 inhibition assays for drug discovery using human liver microsomes with LC-MS, rhCYP450 isozymes with fluorescence, and double cocktail with LC-MS[J]. International Journal of Pharmaceutics, 2007, (08): 126-127
- [6] Wu C T, Yu J C, Yeh C C, et al. Preincisional Dextromethorphan Treatment Decreases Postoperative Pain and Opioid Requirement after Laparoscopic Cholecystectomy[J]. Anesth Analg, 2010, 88:1331-1334
- [7] Dawson GS, Seidman P, Ramadan HH. Improved postoperative pain control in pediatric adenotonsillectomy with dextromethorphan[J]. Laryngoscope, 2009, 111: 1223-1226
- [8] Helmy SA, Bali A. The effect of the preemptive use of the NMDA receptor antagonist dextromethorphan on postoperative analgesic requirements[J]. Anesth Analg, 2009, 92:739-744
- [9] Henderson D J, Withington B S, Wilson J A, et al. Perioperative Dextromethorphan Reduces Postoperative Pain after Hysterectomy[J]. Anesth Analg, 2009, 89:399-402
- [10] Mei Q, Tang C, Lin Y, et al. Inhibition kinetics of monoclonal antibodies against cytochromes P450[J]. Drug Metab Dispos, 2002, 30(6): 701-708
- [11] Lv Zhi, Zheng Yali, Jiang Xingtang. Dextromethorphan reduces false-positive rate in bronchial provocation test with histamine[J]. Chinese Journal of New Drugs, 2011, 22:78-80
- [12] Irwin RS, Curley FJ, French CL. Chronic cough-the spectrum and frequency of causes, key components of the diagnostic evaluation, and outcome of specific therapy[J]. American Review, 2010, (2):399-401
- [13] Zhang W, Han FT, Guo P, et al. Simultaneous determination of tolbutamide, omeprazole, midazolam and dextromethorphan in human plasma by LC-MS/MS-A high throughput approach to evaluate drugdrug interactions[J]. Journal of Chromatography, 2010, (2):108-110
- [14] Atul Kumar, Henry J. Mann, Rory P. Rimmel. Simultaneous analysis of cytochrome P450 probes-dextromethorphan, flurbiprofen and midazolam and their major metabolites by HPLC-mass-spectrometry/fluorescence aRcr single-step extraction from plasma[J]. Journal of Chromatography, 2009(5):1202-1204
- [15] Zhang Xue-kang, Xiong Hui. Different dose of dextromethorphan preemptive analgesia on postoperative pain of remifentanyl anesthesia effect [J]. Journal of Jiangxi Medical College, 2007, 47(5): 79-83
- [16] Chen Xiao-guang, Bai Jie, Sun Xue-feng, et al. Effect of preoperative administration of Dextromethorphan on cough reflex during tracheal extubation [J]. Acta Academiae Medicinae Militaris Tertiae, 2010 (21):1121-1124
- [17] Li Meng-meng, Guo Zheng-gang, Zhang Jin-rong. The effect of preemptive use of dextromethorphan on fentanyl demand during postoperative analgesia[J]. The Journal of Clinical Anaesthesiology, 2009, (14):129-133
- [18] Sun Feng-yan, Gao Jun, Zhang Ling-mei, et al. Neuroprotection of dextromethorphan in rat middle cerebral artery occlusion model [J]. Chinese Journal of neurosurgery, 2011, (23):2019-2022

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- 2005:1478-1500
Cao Ze-yi. Chinese Obstetrics and Gynecology[M]. Second edition, Beijing: People's Medical Publishing House, 2005:1478-1500
- [4] 吴晓杰, 刘霞. 腹腔镜与开腹手术治疗卵巢子宫内膜异位囊肿的比较[J]. 中国微创外科杂志, 2005, 5(3):189-191
Wu Xiao-jie, Liu Xia. Laparoscopic versus open surgery for ovarian endometriosis cysts a comparison study [J]. Chinese Journal of Minimally Invasive Surgery, 2005, 5(3):189-191
- [5] Nakagawa K, Ohgi S, Kojima R, et al. Impact of laparoscopic cystectomy on fecundity of infertility patients with ovarian endometrioma[J]. J Obstet Gynecol Res, 2007, 33:671-676
- [6] Brosens IA, Van Ballaer P, Puttemans P, et al. Reconstruction of the ovary containing large endometriomas by an extraovarian endoscopic technique[J]. Fertil Steril, 2005, 66(4):517-521
- [7] 邹斌, 姬爱冬. 腹腔镜手术继发卵巢早衰患者植物神经功能调整的临床研究[J]. 贵州医药, 2006, 30(3):262
Zou Jian, Ji Ai-dong. Clinical Research of Nerve Adjustment of the Patients with Secondary Premature Ovarian under Laparoscopic Surgery [J]. Guizhou Medical Journal, 2006, 30(3):262
- [8] 简萍, 李斌, 张军, 谢岚. 腹腔镜卵巢巧克力囊肿剥除术电凝止血对卵巢储备功能的影响[J]. 实用妇产科杂志, 2009, 25(11):664-666
Jian Ping, Li Bin, Zhang Jun, et al. Influence on Ovarian Reservation with Electric Coagulation in Endometriotic Cystectomy under Laparoscopy [J]. Journal of Practical Obstetrics and Gynecology, 2009, 25(11):664-666
- [9] 王丽娜, 段丽红. 腹腔镜下卵巢巧克力囊肿剥除术中3种止血法对卵巢功能的影响[J]. 临床合理用药, 2009, 2(18):63-64
Wang Li-na, Duan Li-hong. The Influence of Ovarian Function with Three Hemostatic Method of Shelling out Endometrial Cyst of Ovary by Laparoscopic [J]. Clinical Rational Drug Use, 2009, 2(18):63-64
- [10] Eanler I, Bozdogan G, Aybar F. et al. Outcome of in vitro fertilization/ intra-cytoplasmic sperm injection after laparoscopic cystectomy for endometriomas[J]. Fertil Steril, 2006, 85(6):1730-1735
- [11] Tulikangas PK, Smith T, Falcone T, et al. Gross and histologic characteristics of laparoscopic injuries with four different energy sources [J]. Fertil Steril, 2001, 75(4):806-810
- [12] 岳天孚, 主译. 妇科内窥镜手术图解 - 不孕症和妇科手术[M]. 第1版. 天津科技出版翻译公司, 2006:76
Yue Tian-fu. Gynecological Endoscopic Surgery Illustrations-Infertility and Gynecological Surgery [M]. Tianjin science and technology publishing translation company, 2006:76
- [13] Kimura T, Ku sui C, Matsumura Y, et al. Effectiveness of Hormonal Tourniquet by Vasopressin during myomectomy through Vasopressin V1a Receptor Ubiquitously Expressed in Myometrium[J]. Gynecologic and obstetric investigation, 2002, 54(3):125-131
- [14] 张华, 金柯. 垂体后叶素用于腹腔镜下异位妊娠取胚术止血效果观察[J]. 中国计划生育学杂志, 2011, 19(4):228-230
Zhang Hua, Jin Ke. Hemostatic Effect Observation of the Application of Hypophysis in Salpingotomy by Laparoscope [J]. Chinese Journal of Family Planning, 2011, 19(4):228-230
- [15] 邓少婷. 垂体后叶素在妇科腹腔镜手术中的应用 [J]. 中外医疗, 2011, 22:123-124
Deng Shao-ting. The use of Hypophysis in Gynaecology Laparoscope Surgery[J]. China Foreign Medical Treatment, 2011, 22:123-124
- [16] 王洪彩. 垂体后叶素在腹腔镜输卵管妊娠切开术中的应用及对术后生殖功能的影响[J]. 中国内镜杂志, 2011, 17(11):1147-1154
Wang Hong-cai. The use of hypophysis in salpingotomy by laparoscope and its influence on reproduction function after operation[J]. China Journal of Endoscopy, 2011, 17(11):1147-1154
- [17] 陈淑琴, 刘克玄, 张祖威, 等. 腹腔镜下输卵管切开术中垂体后叶素不同使用方法的比较[J]. 中山大学学报(医学科学版), 2008, 29(6):728-732
Chen Shu-qin, Liu Ke-xuan, Zhang Zu-wei, et al. Comparative study of two different methods of hypophysis use during laparoscopic salpingotomy for tube pregnancy [J]. Journal of Sun Yat-Sen University (Medical Science), 2008, 29(6):728-732
- [18] 李晓丽. 垂体后叶素在腹腔镜下子宫肌瘤剔除中的应用[J]. 中国误诊学杂志, 2011, 11(3):573-574
Li Xiao-li. The Use of Pituitrin Combined with laparoscopic cystectomy surgery of uterine fibroids[J]. Chinese Journal of Misdiagnostics, 2011, 11(3):573-574
- [19] Hiroto Shimanuki, Hiroyuki Takeuchi, Mari Kitade, et al. The effect of vasopressin on local and general circulation during laparoscopic surgery[J]. The Journal of Minimally Invasive Gynecology, 2006, 13(3):190-194
- [20] 梅松原, 刘艳庚, 韩秋丽, 等. 垂体后叶素或缩宫素在腹腔镜肌壁间子宫肌瘤剔除术中应用的对比研究[J]. 中国微创外科杂志, 2011, 11(9):801-804
Mei Song-yuan, Liu Yan-geng, Han Qiu-li, et al. Comparison of Pituitrin and Oxytocin for Hemostasis during Laparoscopic Resection of Intramural Hysteromyoma[J]. Chinese Journal of Minimally Invasive Surgery, 2011, 11(9):801-804

(上接第5102页)

- [19] Woolf C J. Evidence for a Central Component of Post injury Pain Hypersensitivity[J]. Nature, 2009, 306:686-688
- [20] Henderson D J, Withington B S, Wilson J A, et al. Perioperative Dextromethorphan Reduces Postoperative Pain after Hysterectomy[J]. Anesth Analg, 2009, 89:399-402
- [21] Reves J G. Educational Considerations for the Clinical Introduction and Use of Remifentanyl[J]. Anesth Analg, 2009, 89:S4-6
- [22] Rosow C E. An Overview of Remifentanyl[J]. Anesth Analg, 1999, 89:S1-3